

Change in Cerebrospinal Fluid Pressure During Pneumoencephalography Under Nitrous Oxide Anesthesia

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An increase in cerebrospinal fluid pressure occurs in dogs and humans anesthetized with nitrous oxide after air has been injected into the cerebral ventricles. The mechanism for the increase in pressure is felt to be due to the difference in blood solubility between nitrous oxide and nitrogen. Nitrous oxide, being 30 times more soluble in blood than nitrogen, is carried to the air-containing ventricles in a greater quantity than the amount of nitrogen that can be carried away from the ventricles. The result is an increased number of molecules within the ventricles and an increase in intraventricular pressure. This pressure increase might prove fatal, especially in an individual whose cerebrospinal fluid pressure is already elevated. Either the avoidance of nitrous oxide anesthesia or the use of nitrous oxide as the contrast gas would eliminate the rise in pressure.

HUNTER¹ and, more recently, Eger and Saidman² have shown that nitrous oxide is carried to a closed air-containing space within the body in greater quantity and at a more rapid rate than nitrogen can be carried away. This results in an increased number of gas molecules within the space. This should also occur within the ventricles after air has been injected for a pneumoencephalogram and might dangerously increase intracranial pressure since the gas is enclosed by a relatively rigid container. To check the validity of this hypothesis, we measured changes in cerebrospinal fluid (CSF) pressure that occurred during pneumoencephalography under nitrous oxide anesthesia.

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Methods

Four mongrel dogs were anesthetized with pentobarbital, 20 mg./kg., intravenously. Following endotracheal intubation, anesthesia was maintained with halothane, 1-2 per cent, and oxygen. To eliminate hypercarbia as a cause of elevated intracranial pressure, the dogs' lungs were ventilated to establish and maintain a P_{CO_2} of 20 mm. of mercury. A polyethylene canula was placed in a femoral artery both for monitoring arterial blood pressure and for withdrawing arterial blood samples for blood gas analysis. P_{CO_2} , P_{O_2} and pH were determined periodically and standard bicarbonate and base deficit or excess were determined from a Siggaard-Anderson nomogram. Base deficit was corrected with appropriate amounts of sodium bicarbonate. A constant infusion of lactated Ringer's solution was given intravenously. Esophageal temperature was monitored with a Telethermometer (Yellow Springs Corp.) and maintained at 37° C.

A 5 cm. no. 20 spinal needle was introduced into the cisterna magna and connected via a nylon catheter to a Statham strain gauge transducer. Arterial and cisternal pressures were continuously recorded on a direct writing polygraph.

Cisternal pressure was first recorded while the dogs' lungs were ventilated with halothane and oxygen. In 2 of the dogs when cisternal pressure had been stable for 30 minutes, 5-10 ml. of CSF were removed and an equal volume of air injected. When cisternal pressure was again stable, 75 per cent nitrous oxide was added to the anesthetic mixture. End-tidal nitrous oxide was collected with an Otis-Fenn-Rahn end-tidal sampler and monitored with a Beckman infrared nitrous oxide ana-

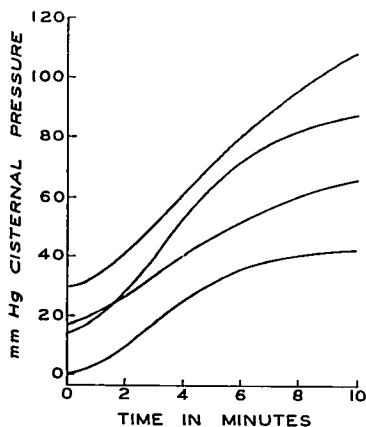


FIG. 1. Rise in cisternal pressure of dogs following the addition of 75 per cent nitrous oxide to the anesthetic at time zero. The cistern was initially filled with air and stable control pressures of from 0 to 30 mm. of mercury were obtained.

lyzer. The nitrous oxide was continued until the cisternal pressure was again stable. At this time, nitrous oxide was discontinued and the cisternal pressure was recorded until it no longer changed. This process was repeated several times in the same dog.

In the third dog, following control pressure measurements with halothane oxygen anesthesia and without injecting air into the cistern, nitrous oxide was added to the anesthetic mixture to determine the effect of nitrous oxide anesthesia on the cerebrospinal fluid pressure. End-tidal nitrous oxide was collected with an Otis-Fenn-Rahn end-tidal sampler and monitored with a Beckman infrared nitrous oxide analyzer. The nitrous oxide was continued until the cisternal pressure was again stable. At this time, nitrous oxide was discontinued and the cisternal pressure was recorded until it no longer changed. This process was repeated several times in the same dog, following which measurements under halothane oxygen anesthesia were repeated, CSF removed, air injected and the experiment continued as in the first 2 dogs.

In the fourth dog, following control pressure measurements under halothane oxygen

anesthesia, nitrous oxide was added to the anesthetic mixture prior to removal of CSF. After a steady cisternal pressure was observed, CSF was removed, an equal amount of nitrous oxide was injected into the cistern, and cisternal pressure was recorded for 30 minutes. Following this, air was injected into the cistern and the pressure observed as in the original experiments.

Similar observations were made on three patients undergoing pneumoencephalography. These patients were premedicated with pentobarbital (Nembutal) and atropine and anesthetized with halothane and oxygen. After succinylcholine was given, the tracheas were intubated with cuffed endotracheal tubes. Ventilation was controlled to eliminate elevated P_{CO_2} as a cause for increased intracranial pressure. A lumbar puncture was performed with the patient in the sitting position and a volume of air sufficient to permit adequate visualization of the ventricles was injected (62, 65, and 55 ml., respectively). When injection was complete, the needle in the lumbar subarachnoid space was connected via a polyethylene catheter to a Statham strain gauge and the CSF pressure continuously recorded. After a stable pressure recording was obtained, nitrous

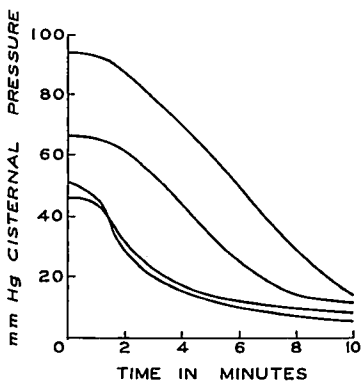


FIG. 2. Decrease in dogs' cisternal pressure following the discontinuation of nitrous oxide anesthesia at time zero. The pressure decrease is delayed for 1-2 minutes because it took this long for the end-tidal nitrous oxide concentration to fall significantly and because of the time delay for nitrous oxide washout from the brain.³

oxide was added to the anesthetic mixture in an inspired concentration of 70-75 per cent. CSF pressure again was recorded until a peak rise was obtained or until this pressure rose to within 20 millimeters of the systolic arterial pressure. At this time, the nitrous oxide was discontinued and the CSF pressure recorded until stable.

Results

Following the removal of CSF and replacement by air, stable cisternal pressure of 0, 17, 18, and 25 mm. of mercury (0, 231, 245, and 330 mm. of water) were obtained in the four dogs. With addition of nitrous oxide to the anesthetic, cisternal pressures rose to 41, 87, 65, and 108 mm. of mercury (557, 1080, 883, and 1470 mm. of water), respectively (fig. 1). These increases all occurred within 10 minutes after the nitrous oxide was begun. Within ten minutes of discontinuing the N_2O , the cisternal pressures fell to less than 20 mm. of mercury (272 mm. of water) in all dogs (fig. 2). The initial drop was delayed for one to two minutes in several of the dogs, both because it took this long for the end-tidal N_2O to drop significantly and because of the time delay for nitrous oxide washout from the brain.³

In several of the experiments, a curious phenomenon was observed. While waiting

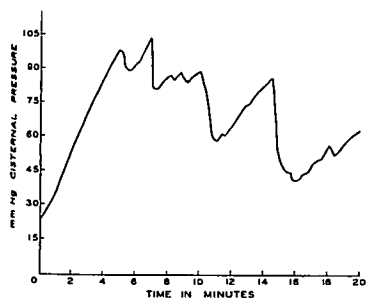


FIG. 3. The "sawtooth" rise and fall in the cisternal pressure of dogs observed during nitrous oxide anesthesia. This might represent a "bubble" of gas or fluid being pushed out of the subarachnoid space through the arachnoid granulations when CSF pressure rose to a sufficiently high value and overcame the interfacial tension between the granulations and the gas.

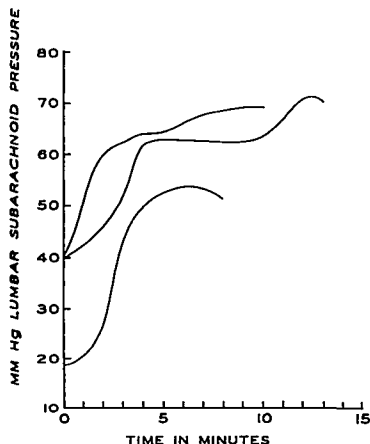


FIG. 4. Rise in lumbar subarachnoid pressure of humans following the addition of 75 per cent nitrous oxide to the anesthetic at time zero. Air had previously been injected into the lumbar subarachnoid space and steady control pressures of from 19 to 39 mm. of mercury had been obtained.

for a peak cisternal pressure to be obtained, there was a sudden rapid fall in cisternal pressure after which it slowly rose again (fig. 3). The "sawtooth" rapid fall and slow rise repeated itself several times. Welch⁴ has shown that the arachnoid granulations are actually microscopic channels that act as one-way valves and allow cerebrospinal fluid to flow from the subarachnoid space into the superior sagittal sinus, but prevent the flow of blood in the opposite direction. The flow of fluid is increased by an increase in perfusion pressure. There is a critical opening pressure at which flow through the channels begins. This opening pressure is related to the interfacial tension between the wall of the channel and the fluid. In our study we postulate that although the flow of cerebrospinal fluid through the arachnoid granulations was occurring and probably increasing as the pressure rose, a higher opening pressure was needed for the passage of a gas bubble. This is because of the higher interfacial tension between the channel wall and the non-wet gas phase within the ventricle. When this higher pressure was reached, a bubble of gas escaped, thus lower-

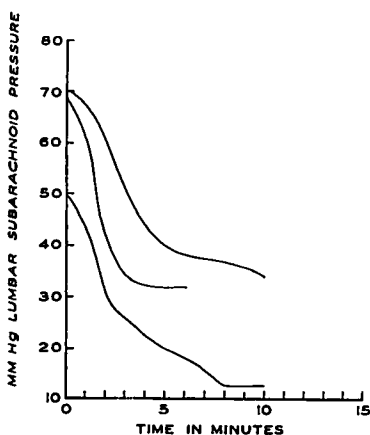


FIG. 5. Fall in human lumbar subarachnoid pressure following the discontinuation of nitrous oxide anesthesia at time zero.

ing the intraventricular pressure. It is only when the pressure rises again that another bubble of gas escapes. These bubbles of gas must be small, and being mixed with returning venous blood are probably not a hazard as emboli.

When nitrous oxide was administered before air was injected into the cistern, no change in cisternal pressure was observed.

If nitrous oxide rather than air were injected into the subarachnoid space while the dog was breathing nitrous oxide, a slight fall in cisternal pressure was seen.

The results of the studies in man are seen in figure 4. Initial pressures were generally higher (19, 39, 39 mm. of mercury or 258, 530, and 530 mm. of water) than they were in the dogs because with the patient in a sitting position, the hydrostatic pressure of a column of CSF was added to the pressure in the ventricles. When nitrous oxide was administered, there was a rise in CSF pressure that was similar although quantitatively less than that which occurred in the dogs (fig. 4). Peak pressures of 53, 69, and 71 mm. of mercury (720, 937, and 966 mm. of water), respectively, were obtained. Discontinuance of nitrous oxide resulted in a return of CSF pressure to below

the previous control readings within ten minutes (fig. 5).

Discussion

These results are consistent with previous investigations into the phenomenon of gaseous exchange in and out of air spaces within the body. Hunter¹ reported small increases (7 cm. of water) in intrapleural pressure occurring in patients receiving nitrous oxide who had prior therapeutic pneumothorax. He concluded that the pressure rise was due to the fact that nitrous oxide, because of its high blood gas solubility compared to nitrogen, was brought to the pleural cavity faster than the nitrogen was removed. The rise in intrapleural pressure that Hunter reported was small because of the high compliance of the intrapleural cavity. As a result, an increase in volume rather than pressure was the predominant change.

Tenney³ injected sulfur hexafluoride, a gas with a lower blood gas solubility than nitrogen, into the peritoneal cavity of dogs and cats and observed a rise in volume of peritoneal gas. In this case nitrogen, having a higher blood gas solubility than SF₆, was carried to the peritoneal cavity in greater quantity than SF₆ was carried away.

We believe that the following sequence takes place in the cerebral ventricles during air contrast studies under nitrous oxide anesthesia. A volume of air is injected into the subarachnoid space and rises to the ventricles. The gas in this air is composed of nitrogen and oxygen with the partial pressure of nitrogen being approximately 600 mm. of mercury. The blood that circulates through the walls of the ventricles carries nitrous oxide at a partial pressure of about 550-600 mm. of mercury (depending on the percentage of nitrous oxide administered) and essentially no nitrogen. Therefore, a gradient exists between the air in the ventricle and the blood for both nitrous oxide and for nitrogen. Thirty times more nitrous oxide than nitrogen can be carried in the blood at the same partial pressures because the blood gas solubility coefficient of nitrous oxide is thirty times that of nitrogen (table 1). Thus, initially, a greater number of nitrous oxide molecules can be given up by blood to the ventricles, compared to the number of

nitrogen molecules removed. The result is an increase in the total number of gas molecules within the ventricles. Since the compliance of this intracranial space is limited because of the skull, the pressure must rise. If no nitrogen were lost and if the compliance were zero, then at equilibrium the intracranial pressure would increase by 550-690 mm. of mercury. This maximum pressure increase does not occur for the following reasons: (1) some nitrogen is absorbed, (2) cerebrospinal fluid and gas are lost through the arachnoid granulations, and (3) vascular channels can be compressed.

When nitrous oxide is discontinued, a reverse in gas exchange occurs. The partial pressure of nitrous oxide in blood falls to zero; and the nitrous oxide, because of its high blood solubility, is rapidly carried away from the ventricles. At the same time, even if the patient is breathing air, only a small amount of nitrogen can be carried to the ventricles because of the low solubility of nitrogen in blood. The end result is a decrease in the number of gas molecules within the space and a decrease in CSF pressure.

The pressure increase will occur with any relatively soluble agent that is given in a high percentage or partial pressure (*i.e.*, N₂O, ethylene, xenon). Rise in pressure with ethylene or xenon would probably be somewhat less rapid and less extreme than with N₂O because of the lower blood solubility of these gases.

The increase in pressure can be largely avoided if one of several things is done. First, one could avoid using an anesthetic such as nitrous oxide that must be administered in high concentration. However, if nitrous oxide anesthesia were used, the injection of nitrous oxide instead of air into the ventricle would eliminate the gradient from blood to ventricle and prevent transfer of gas molecules into the ventricle. At the end of the procedure, when the nitrous oxide anesthesia was discontinued, the partial pressure of nitrous oxide in the blood would fall to zero, and nitrous oxide in the ventricle would be rapidly removed by the blood. The end result would be the rapid disappearance of the intracranial gas space.

A further advantage in the use of a soluble gas such as nitrous oxide rather than air for

TABLE 1: Blood/Gas Partition Coefficients of Gases That Might Be Present in the Blood at High Partial Pressures

Agent	Blood/Gas Partition Coefficient
Nitrous oxide	0.468 ⁶
Nitrogen	0.0137
Ethylene	0.140 ⁸
Xenon	0.20 ⁹
Cyclopropane	0.415 ¹⁰

encephalography would be the decreased incidence of post pneumoencephalographic headache. The severity and duration of these headaches appear to correlate with the length of time that injected gas remains in the ventricles.¹¹ Aird has reported that in dogs, ethylene injected for encephalographic studies disappeared within two hours and N₂O within an hour, while air remained for seven days.¹² Newman¹³ used ethylene for 30 pneumoencephalograms and noted a markedly decreased incidence of postinjection headache. The use of nitrous oxide or ethylene as the contrast gas resulted in roentgenograms that were perfectly satisfactory.

Deaths associated with pneumoencephalography have been reported to occur in an incidence from 0.22 per cent¹¹ to 8.17 per cent.¹⁴ When autopsies are performed to ascertain the cause of death, the most frequent diagnoses are air embolism or death secondary to the disease process for which the contrast study was being performed. In a number of cases, however, the cause of death is obscure. An increase in intracranial pressure necessitates an increase in arterial blood pressure to perfuse the brain. It is possible that if a patient already has increased intracranial pressure, he may be unable to compensate for a further rise in intracranial pressure and cerebral ischemia may result. This rise in intracranial pressure might also lead to cerebral congestion and edema on the basis of venous obstruction.

The following is a report of a death that seems to fall into the pattern of this discussion. A 4 month old child underwent pneumoencephalography. Except for radiologic evidence of increased intracranial pressure (spreading of the sutures), there were no abnormal neurological findings. Anesthesia was induced and maintained with nitrous oxide oxygen 3:1 liters/minute and halo-

thane 1 per cent through an Ayre's T-piece. Endotracheal intubation was accomplished with ease following which the child was placed in the sitting position. A lumbar puncture was performed and 37 ml. of air were injected into the subarachnoid space without removal of fluid. Ten minutes later, respirations suddenly ceased and the pulse, which had been stable at 120, suddenly fell to 65. Upright roentgenograms were taken during this sudden change in status following which the child was placed in the supine position. At this time, pulmonary edema was noted. This was successfully treated with pulmonary positive pressure oxygen, tourniquets, and rapid digitalization. However, the child expired shortly afterward. Autopsy revealed an organizing subdural hematoma, a cerebral contusion, and evidence of pulmonary edema. The roentgenograms that had been taken showed air in the ventricles as well as the subdural space.

The probable circumstances leading to this child's death are: (1) he had increased intracranial pressure, (2) this was further increased by the injection of air into the ventricles, and (3) increased further by nitrous oxide. The final intracranial pressure was not tolerated by this child, as evidenced by the apnea, bradycardia, and pulmonary edema.

We have demonstrated in dogs and in human beings that a rise in intracranial pressure does in fact accompany pneumoencephalography under nitrous oxide anesthesia. Since the mortality associated with this procedure is low, the rise in pressure is apparently well tolerated by the majority of patients. However, we feel that the occasional unexplained death associated with pneumoencephalography (such as reported here) may result from the cerebral ischemia and consequent brain damage, and/or profound hypertension and pulmonary edema due to increased intracranial pressure.¹⁵ It is for this reason that we feel that nitrous oxide anesthesia is contraindicated during air encephalography.

Summary

Nitrous oxide anesthesia during or following the injection of air into the cerebral ventricles has been shown to result in an increase in cerebrospinal fluid pressure. The mechanism for the increase in pressure is attributed to the high blood solubility of nitrous oxide compared to that of nitrogen. The difference in solubility results in a greater number of nitrous oxide molecules entering the ventricles than

the number of nitrogen molecules that leave. This gaseous exchange can be eliminated if nitrous oxide rather than air is injected into the ventricles.

We believe that the rise in cerebrospinal fluid pressure may be the reason for the occasional unexplained fatality that occurs during pneumoencephalography, and for this reason nitrous oxide is contraindicated as an anesthetic for pneumoencephalography.

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